ABSTRACTS

* **Uptake and Toxicity of Respirable Polyester Fiber Particles following UV Weathering**

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Abstract:
Air pollution during the critical periods of climate change can drive the development of respiratory diseases by increasing oxidative stress and inflammation in the lung. Climate change can increase climatic stress factors (i.e. UV radiation and temperature extremes) and cause oxidative alterations to the surface physicochemistry of air pollutants. Respirable microplastics and fibers in air particulates may be subjected to such environmental weathering. The documentation of occupational respiratory diseases in synthetic textile workers and the recent evidence on the presence of fibers in human lung tissue exacerbate the concern about fibers cytotoxicity and inflammation in the lung. Here, we evaluated the physicochemical characteristics and toxicity of fiber particles from a fleece polyester fabric before and after UV weathering by integrating microscopy, spectroscopy, and cytotoxicity. Raman spectroscopy confirmed that the chemical structure of leached particles from the fleece blanket matches with polyester microfibers. Scanning electron microscopy energy-dispersive spectroscopy and Raman spectroscopy revealed the increase in the concentration of metals impurities (i.e. titanium and silica) on the surface of UV-aged particles and the decrease in the intensity of the allenes group respectively. Carbonyl, ketone, and carboxylic functional groups increased on the near-surface region of UV-aged particles as indicated by X-ray photoelectron spectroscopy. Both fresh and UV-aged fibers of respiratory sizes induced dose-dependent cytotoxicity. UV radiation amplified fiber particles cytotoxicity by increasing 10 % the cell mortality at 500 µg/ml particles concentration, in comparison to fresh fibers. Transmission electron microscopy identified the intracellular translocation of UV-aged particles at 50 µg/ml particles concentration. Our study highlights the importance of understanding the environmental health risks from fiber particles exposure and their implications for the inflammatory mechanisms in the lung.

* **Thinking Zinc: An Intervention to Address Environmental Metal Exposure on the Navajo Nation**

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Abstract:
More than 500 abandoned uranium mines (AUMs) are located on the Navajo Nation and previous studies find an increased risk for chronic diseases related to AUM waste exposure. Experimental models demonstrate that metals such as uranium and arsenic disrupt certain zinc finger motifs and affect protein function: supplemental zinc confers protection against the metal effects. Based on this evidence, a community and academic partnership developed an intervention trial called Thinking Zinc. Thinking Zinc tests the hypothesis that dietary zinc supplementation at the recommended daily allowance will modulate biomarkers of oxidative stress, inflammation and immune dysregulation, and decrease DNA damage in a metal-exposed population. Extensive community engagement and collaboration informed study name, study design and ensured that Thinking Zinc is congruent with Navajo cultural values. The study is a single-arm cohort design with longitudinal collection of biospecimens. Urinary metal analysis finds Thinking Zinc study participants with elevated levels of uranium approximately 4- fold greater than those detected in the general US population. Of 15 metals tested, 4 had at least 10% of the participants above the National Health and Nutrition Examination Survey (NHANES) 95th percentile. Interestingly, the median values of multiple metals were lower in the Thinking Zinc group compared to the Navajo Birth Cohort Study. Urinary metals differences were observed between the two study locations, Red Water Pond Road and Blue Gap/Tachee. Many metals show substantial fluctuations over time, with greater differences detected in urinary versus serum metals. Median total urinary arsenic concentrations in Thinking Zinc participants are similar to values in NHANES, although there are distinct differences in arsenic forms suggesting changes in metabolic outcomes for arsenic in the Navajo population. Zinc did not appreciably affect urinary levels of measured metals with the exception of uranium. Zinc supplementation modestly decreased serum copper and increased serum selenium with both pre- and post- zinc levels within the reference ranges. Analysis of biomarkers pre- and post-zinc supplementation reveals a decrease in oxidative damage to lipids and DNA. Expression of some cytokines was modified after zinc supplementation. These preliminary findings suggest there may be benefits of zinc in a population exposed to AUM waste.

* **Zinc Supplementation Alters Tissue Distribution of Arsenic in *Mus musculus* with Corresponding Changes in Metal Transporters**

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Abstract:
Arsenic (As) exposure is a global concern because it is found at elevated levels in contaminated soil and water supplies. The As from these sources can find its way into the human body through ingestion of foods grown in contaminated soils, dust inhalation, and consumption of tainted water. Prolonged exposure to elevated levels of As have been linked to a variety of diseases including cardiovascular disease, skin disorders, immune disorders, neurotoxicity and cancer. A variety of mitigation strategies have been used to combat As

exposure however zinc (Zn) supplementation remains a possible therapeutic option that requires further study. Cell-based studies have shown that Zn supplementation is able to counteract some of the molecular impacts of As exposure. To investigate the distribution of As and Zn in different tissues and the alterations in tissue distribution when given combination treatment, mice were exposed to 5 ppm sodium arsenite, 10 ppm zinc chloride, or a combination of the two in drinking water for a total of six weeks. Plasma, liver, spleen, and kidney tissues were harvested for ICP-MS analysis to evaluate As and Zn concentrations and qRT-PCR was performed to analyze changes in known As and Zn transporters. As treatment alone significantly increases the amount of As in all tissues while Zn supplementation alone did not alter the amount of Zn in any of the tissues. However, Zn supplementation decreased the levels of As in plasma, liver, spleen, and kidney. Highlighting possible causes of these results, in the liver the decreased accumulation of As in the presence of supplemental Zn corresponds with an increase in *Mrp1* (a known As(GS)III exporter) expression. This increase is only seen in the presence of both metals. As treatment did not cause liver damage as measured by serum Alt-1. In the spleen, supplemental Zn increases expression of *Glut1*, which when combined with As exposure may assist in the reduction of arsenicals. In the kidney, As and Zn treatments individually decrease the expression of *Aqp9* (transporter that causes the efflux of methylated arsenic metabolites) and the result is additive in the combination treatment. The enhanced reduction of *Aqp9* may contribute to the reduced tissue arsenic observed in the combination treatment. Of note, As treatment alone decreases the amount of Zn in the kidney and when supplemental Zn is given, the Zn concentration in the tissue returns to normal. This phenomenon corresponds to an increase in expression to *Zip10* (a Zn importer) and *Mrp2* (an arsenic exporter). Results from this study demonstrate that Zn supplementation can lower As accumulation in a variety of tissues, which may in turn lessen the negative impacts of arsenic exposure.

* **Title: Arsenic Acts as a Co-mutagen by Affecting the Somatic Mutations Imprinted by Ultraviolet Light**

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Abstract:
Although arsenic alone induces cancers in the lung, bladder, kidney, and skin, it is also a potent co-carcinogen. Studies suggest arsenic enhances UVR skin cancer, but the mechanisms are not fully understood. One proposed mechanism is inhibition of the nucleotide excision repair (NER) pathway, which is responsible for repairing cyclobutane-pyrimidine dimers (CPDs), a type of UVR DNA damage that results in mutations found in UVR skin cancers. Carcinogenic mechanisms can be explored using mutational signatures analysis, a novel whole genome sequencing approach that associates mutation patterns with specific molecular mechanisms. UVR mutational signatures are well defined, but no studies have used mutational signatures to investigate co-carcinogenesis. In this study two models, human skin

cells and SKH-1 mice, were co-exposed to arsenic and UVR to investigate arsenic-altered mutation patterns of UVR exposure. Arsenic alone did not induce mutations, but significantly increased UVR mutations and altered the spectra of select UVR mutational signatures. The proposed UVR indel mutational signature, ID13, is only found in a subset of skin cancers. As the first study to investigate co-carcinogenesis we found ID13 in arsenic-UVR co-exposed groups but not UVR alone groups indicating ID13 may be unique to arsenic-UVR co-exposure and may serve as a biomarker of arsenic and UVR co-exposure. These findings show arsenic alters select mutational processes of UVR carcinogenesis and demonstrates mutational signatures is a novel tool to investigate metal carcinogenesis.

* **Adipocyte Number and Adipokine Secretion in the Bone Niche Shifts in Response to Tungsten Exposure in Both Nontumor and 4T1 Breast Tumor-Bearing BALB/c Mice**

Author Block: C. M. McVeigh, C. J. Chock, S. Templeton, C. V. Nguyen, and A. M. Bolt. *University of New Mexico, Albuquerque, NM.*

Abstract:
Tungsten is classified as an emerging environmental toxicant due to increasing exposure and lack of knowledge about the human health risks. Epidemiological and *in vivo* studies have demonstrated that exposure to tungsten contributes to the carcinogenic process. However, there is a gap in knowledge in our understanding of how tungsten drives these processes. Due to a cohort of breast cancer patients accidentally exposed to tungsten during intraoperative radiotherapy, our lab is currently investigating the effects of tungsten exposure on breast cancer progression and metastasis. Tungsten is known to accumulate within the bone, creating a site for long-term exposure and toxicity. Breast cancer is also known to metastasize to the bone. We have previously shown, using the 4T1 orthotopic breast cancer model, that oral tungsten exposure enhances metastasis, osteolysis and myeloid-derived suppressor cells in the bone niche. These findings suggest that tungsten deposition in the bone creates a favorable microenvironment to promote metastasis. Bone marrow adipocytes (BMA) play an important role in breast cancer metastasis to the bone through the secretion of adipokines that drive tumor cells homing, colonization, and growth by changing the microenvironment. In order to investigate the role of BMA in tungsten-enhanced breast cancer metastasis in the bone, we quantified the number of Plin1+ (Perilipin-1) adipocytes and evaluated the gene expression of adipokines in both non-tumor and 4T1 tumor-bearing BALB/c female mice exposed to either tap water or tungsten in the drinking water (15 ppm, 8 weeks). We found that the overall burden of Plin1+ adipocytes within the bone marrow niche was increased in the non-tumor bearing, tungsten-exposed mice. In the 4T1 tumor-bearing mice, tungsten exposure also slightly increased the number of Plin1+ adipocytes, however the overall number of adipocytes were significantly decreased. Tungsten exposure also shifted the adipokine profiles in the bone marrow niche, in both non-tumor and 4T1 tumor-bearing mice. Interestingly, the adipokines that were elevated following tungsten exposure in each group were different. Non-tumor bearing mice, tungsten increased expression of *Adipoq, Cxcl10, Fabp4, Il-6,* and *Sdf1* while 4T1-tumor bearing mice, tungsten increased expression of *Cxcl2*, *Il-1β*, and *Tnfα* and decreased expression of *Adipoq*.

These results suggest that adipocytes could be important mediators driving tungsten-enhanced breast cancer metastasis to the bone. Future work will focus on investigating how changes in bone adipocytes following tungsten exposure contribute to this process. *Funding P20GM130422.*

* **Utilizing a Human Lung Epithelial Cell Macrophage Co-culture Model to Assess the Effects of Environmental Toxicants *In Vitro***

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Abstract:
The development of representative *in vitro* models to investigate the effects of inhalation exposure of the lung environment to particulate matter is an essential step in the inhalation toxicology field. The inhalation of particulate matter from environmental sources such as vehicular sources, energy production, mine dusts as well as microplastics contributes to increased rates of diverse diseases, such as autoimmunity, hypertension, and interstitial lung diseases. While A549 cells are routinely used as a model for the testing of the effects of toxicants in the lungs, there is insufficiency in the representation of these cells to model the lung environment due to the lack of important immune cell populations and the inability to model the effects of their response and recruitment to sites of exposure. The addition of differentiated THP-1 monocytic cells into macrophages onto A549 cells in a co-culture model helps to investigate the interactive responses to deposited particulates as an immune-epithelial interface. We developed this model to investigate toxicity endpoints following particulate exposure *in vitro*. For the mine dust studies the A549 and THP-1 macrophages were plated in a 10:1 ratio and cells were exposed for 24-48-hours to soluble arsenic (6/12µM) and vanadium (60/120µM), with and without the addition of aluminum silicate powder (20µg). Aluminum silicate comprises roughly 25% of the mine dust from abandoned mine site waste in the four corners area of the United States, so we sought to determine whether there was a compounding effect of the aluminum silicate in combination with the heavy metals present in the mine dust. Analysis of the co-culture after treatment with the metals +/- silicate was performed by flow cytometry where a CD45 antibody was utilized to distinguish the macrophages from the epithelial cells. Markers for DNA damage and cytotoxicity-phosphorylated γ-H2AX and Live/Dead staining were also included in the panel. The results indicated that within the co-culture there was a differential toxicity response where the epithelial cells showed no change in DNA damage after treatment with arsenic or vanadium, yet the macrophages showed a significant increase in DNA damage after the arsenic treatment. Interestingly co-treatment with silicate did not magnify the effects of arsenic alone. At these short timepoints no cytotoxicity was observed in any of the treatment groups. Concurrent studies on the effects of microplastics on the co-culture tight junctions through Electric Cell-substrate Impedance Sensing (ECIS) showed a decreased level of resistance with the addition of the macrophages to the epithelial monolayer, as well as a significant decrease in resistance when the co-culture was treated with microplastics over the epithelial cells treated with microplastics in a monolayer. In order to further study the effects

of these microplastics on the co-culture, high content imaging will be utilized with a stain for Claudin-V as well as Phalloidin to further discern the cause for the decreased resistance in the co-culture model after the microplastic treatment. This coculture model enables insights into the relationships between major cell types in the immune defense against environmental particulates

* **Identification and Quantitation of Microplastics Exposure in Human Placenta**

Author Block: M. Garcia[1], E. Castillo[1], E. Barrozo[2], M. Suter[2], G. Herbert[1], S. Lucas[1], D. Scieszka[1], E. El Hayek[1], J. Gonzalez-Estrella[3], A. Konya[3], K. Aagaard[2], and M. Campen[1]. *[1]University of New Mexico, Albuquerque, NM; [2]Baylor College of Medicine and Texas Children's Hospital, Houston, TX; and [3]Oklahoma State University, Stillwater, OK.*

Abstract:
Global plastic use has exponentially increased over the past century, and microplastic (MP) pollution and ingestion are emerging environmental issues with uncertain impacts on human health. There is a significant knowledge gap in the quantitation of systemic uptake and distribution of ingested or inhaled microplastics (MPs), which limits our appreciation for potential health effects. MPs ultimately enter the ecosystem and become inhaled or ingested by both animals and humans, potentially leading to toxicity and adverse health outcomes. This study focuses on the impacts of MPs and establishes how they accumulate within the placenta during gestation. We obtained frozen, uniformly collected and banked placenta samples from PeriBank, Baylor College of Medicine and Texas Children's Hospital's perinatal biorepository from 81 subjects. Samples were analyzed for MP accumulation using complementary techniques to identify, isolate, and quantify MPs to aid in the early identification of MP-associated placental health outcomes associated. Placenta samples were weighed, and tissue digestion was performed with 3x the tissue volume using 10% KOH, incubated at 40^{o}C for 72 hours with agitation, and ultracentrifuged for 4 hours at 30,000g. MP accumulation was determined by weight of the resulting pellet formed, normalized to compositional distributions determined by micro-FTIR spectroscopy. Further analysis included using confocal microscopy, which revealed significant translocation of MPs and fibers into the placenta. We also utilized micro-FTIR to establish the number of particles detected and the identification of particle types in the placenta samples. Results showed an average of 2.33 (±0.58) fibers, 16 (±1.73) fragments, and 80.33 (±3.21) particles per sample, and a mass concentration range of 0.1-4 mg/g of placenta. We identified the highest concentrations to be rayon, polystyrene, and polyethylene (olefin). Complete quantitation of plastics concentration in placental tissues is further enabled by dissolution in nonpolar solvents and gas chromatographic assessment. This study shows further evidence that MPs are ubiquitous in human placental samples and provides important information related to size, shape, and composition of contaminant materials. Future research will explore the influence of MPs on gestational health.

* **Sex-Dependent Inflammatory Sequelae and Mechanisms following Acute Wood Smoke Exposure**

Author Block: K. E. Zychowski, M. Grimes, Q. Jacquez, A. Camacho, C. Dixson, and S. Yazzie. *University of New Mexico, Albuquerque, NM.*

Abstract:
Episodic wildfire events are a growing global concern due to climate change and drier weather conditions. The full-scope of sex-dependent, inflammatory consequences and mechanisms following woodsmoke (WS) exposure is currently unknown. In this study, we exposed male and female C57BL/6 mice to either filtered air (FA) or WS for 4h/d for 2 d, to simulate an acute, wildfire event in a pre-clinical rodent model (n=8 per group). In a second set of studies, we ovariectomized female mice to evaluate acute WS toxicity in a model of ovarian hormone depletion/menopause. Woodsmoke exposures averaged 0.575±0.12mg/m^3 per day, with significantly increased ($p<0.05$) levels of Ni, Ag, W and U in analyzed WS particulate matter, compared to FA. In the bronchoalveolar lavage fluid (BALF), females demonstrated significantly ($p<0.05$) diminished protein expression in IL-10, and IL-6 following WS exposure compared to FA, whereas males did not show any changes. Males, however, showed significantly fewer BALF macrophages following WS exposure, and greater glial fibrillary acidic protein (GFAP) staining in the cortex compared to FA-males. There were significantly increased levels of lung mRNA IL-1β, TNF-α, and IL-6 in female, WS-exposed mice, compared to males. Brain hemispheres demonstrated elevation of genes including IL-1β, CXCL-1, TGF- β and IL-6 in males exposed to WS, compared to females. In addition, lipidomic assays indicated greater phenotypic changes in females than in males in both plasma and brain samples, following WS exposure. Sex and exposure (FA/WS) demonstrated statistically significant interactions across several biomarkers tested, based on 2-way ANOVAs. Ovariectomized (OVX) mice exposed to WS revealed significantly greater inflammatory responses in lung, bone marrow and the CNS compared to Sham mice. These inflammatory impacts demonstrate statistically significant interactions, between sex and exposure treatment, which may be mechanistically based on ovarian presence in females.

* **Neurotoxicity Is Sex-Dependent following Acute Wood Smoke Exposure**

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Abstract:
Acute woodsmoke (WS) exposure is a growing concern due to climate change and the increase in episodic wildfire events. The full-scope of sex-specific, physiological consequences is currently unknown, including neurological responses to WS. In this study, we exposed C57BL/6 male and female mice to either filtered air (FA) or WS for 4h/d for 2 d, to simulate an acute, wildfire event in a pre-clinical rodent model (n=8 per group). Woodsmoke exposures averaged 0.575±0.12mg/m^3 per day. Metals assessment in WS filters demonstrated a statistically significant ($p<0.05$) upregulation of Ni, Ag, W and U, compared to FA filters. Woodsmoke-exposed males showed a significant increase in glial fibrillary acidic protein (GFAP) staining, a marker of reactive astrocytes, in the cortex and increased IL-1ß, IL-

6, TGF- ß, and CXCL-1 mRNA gene expression in brain hemispheres, compared to WS-exposed females. These impacts demonstrated a statistically significant interaction between sex and exposure treatment, based on a two-way ANOVA with Tukey's post-hoc test ($p<0.01$). Interestingly, targeted lipidomics analyses of both brain and plasma samples in males and females indicated consistent significant decrease in several phosphatidylethanolamine (PE) and phosphatidylcholine (PC) lipids following WS exposure. Furthermore, preliminary assessment of circulating small extracellular vesicles (sEVs) show significantly increased inflammation (CXCL-1, IL-6 mRNA) in mouse cerebrovascular cells (mCECs) driven by WS-sEVs and increased mCEC uptake of serum-borne WS-sEVs, *in vitro*, compared to the FA-group in both males and females ($p=0.01$). Data demonstrate that this effect is not contingent on clathrin-mediated endocytosis. In conclusion, several neurotoxic impacts following WS exposure are sex-dependent responses, predominantly based on inflammatory processes.

* **Immune Surveillance and Exploratory Molecular Pathway Analysis in Miners: A Rural-Based Pilot Study**

Author Block: Q. Jacquez[1], E. Erdei[1], X. Zhou[1], C. Shuey[2], A. Camacho[1], N. Ass'ad[1], K. Page[1], B. Gore[3], C. Zhu[4], A. Sood[1], and K. Zychowski[1]. *[1]University of New Mexico, Albuquerque, NM; [2]Southwest Research and Information Center, Albuquerque, NM; [3]Miners' Colfax Medical Center, Raton, NM; and [4]Department of Immunology and Microarray Core, Dallas, TX.*

Abstract:
There is an extensive history of mining including coal, metals, and uranium (U)-mining in the Southwest region of the United States. Research has shown that specific ore miners, such as U-miners, are at a greater risk for developing autoimmune diseases including systemic sclerosis and systemic lupus erythematosus (SLE). Currently, autoimmune biomarkers are widely understudied in miners. Therefore, more research is needed to understand which signaling pathways may play a role in this occupational- driven autoimmunity. In this project, a rural pilot study was conducted with a mobile clinic platform to assess autoimmune biomarkers in miners. The miners self-identified as either U (n=10) or non-U miners (n=34) and were given routine health screenings. Preliminary screening for immune-related molecular dysfunction used high-throughput molecular technique to assess IgG and IgM serum-borne autoantibody markers. Three histone IgM autoantibodies (histone H2A, H4, H3) and spliceosomal proteins, SmD1/D2/D3, were downregulated in the U-miners, and alpha-actinin IgM was upregulated in the U-miners, relative to the non-U miner's group. The survey of both U- and non-U miners using bioinformatics-based, signal pathway analysis revealed significant signaling alterations in several key histone-related proteins (H1-0, H2BC21, H2AC15). Even when adjusting for age as a covariate, using multivariable modeling, there was a significant association ($p<0.05$) between U-mining and biomarkers including IgM alpha-actinin, entactin, histones H1, H2B, and H4, myeloperoxidase (MPO) and myelin basic protein and IgG myelin basic protein, cytochrome C and human centromere protein A (CENP-A). Additional research is necessary to further understand the mechanistic connection between U-exposure, autoantibody development, specifically IgM and histone-related alterations.

* **Arsenic (+III Oxidation State) Methyltransferase Is an Important Mediator of Arsenite-Induced Hematotoxicity in Male Mice**

Author Block: L. V. Santos-Medina[1], H. Zhang[2], Z. A. Yee[1], K. J. Martin[1], G. Wan[2], A. M. Bolt[2], X. Zhou[2], M. Stýblo[3], K. J. Liu[2], and S. Medina[1]. *[1]New Mexico Highlands University, Las Vegas, NM; [2]University of New Mexico, Albuquerque, NM; and [3]University of North Carolina at Chapel Hill, Chapel Hill, NC.*

Abstract:
Human exposures to environmental metals such as arsenic are a worldwide public health concern. Chronic exposures to arsenic are linked to many health effects including anemia. Epidemiological studies in populations chronically exposed to arsenic have shown that methylation capacity, mediated by the arsenic (+III oxidation state) methyltransferase (As3MT) enzyme, is associated with elevated disease risk. Arsenic metabolism has an important role in detoxification, but it also generates bioactive intermediates with toxicity that may be greater than the parent inorganic arsenicals. Many studies suggest that the metabolites generated though the biotransformation of arsenite (AsIII), including monomethylarsonous acid (MMAIII), may be the primary arsenicals responsible for toxicity *in vivo*; however, few studies have been performed to directly evaluate this. In the present study, we used male *As3mt*-knockout (KO) and wildtype, C57BL/6J, mice to evaluate the role of arsenic biotransformation in the development of anemia following drinking water exposures to AsIII. We found that exposure to 1 mg/L (ppm) AsIII for 60 days resulted in the significant reduction of red blood cell counts, hematocrit, and hemoglobin levels in the blood of wildtype, but not *As3mt*-KO mice. In support, we also observed significantly elevated levels of circulating erythropoietin in the serum of wildtype mice. Collectively, results from this study suggest that the process of arsenic biotransformation may have a critical role in mediating the hematotoxicity of arsenic. *This work was supported by the National Institutes of Environmental Health Sciences (NIEHS) Grant Number RO1 ES029369, R01 ES029369-03S1; National Institute of General Medical Sciences(NIGMS) of the National Institutes of Health (NIH) Grant Number 1R16GM146669-01, P20 GM130422, Institutional Development Award (IDeA) P20 GM103451; NIEHS and UNM METALS Superfund Research Program Grant Number P42 ES025589; UNM Center for Metals in Biology and Medicine (CMBM) through NIH, and the National Science Foundation Louis Stokes Alliance for Minority Participation, Undergraduate Research Scholars Program.*

* **Impacts of Polystyrene Microplastics on the Growth, Survival, and Macrophage Differentiation of Human THP-1 Monocytes**

Author Block: K. J. Martin, A. M. Baca, L. V. Santos-Medina, Z. A. Yee, and S. Medina. *New Mexico Highlands University, Las Vegas, NM.*

Abstract:
Microplastics (MPs) are environmental pollutants of increasing concern for human health.

Humans are exposed to MPs in a variety of ways including through drinking water. However, the immune and other health issues associated with MPs exposures remain largely unknown. In the present study, the human monocytic cell line, THP-1, was exposed *in vitro* to increasing concentrations (0.1 µg/mL, 1 µg/mL, 10 µg/mL, and 100 µg/mL) of 1 µm and 5 µm polystyrene MPs, as well as mixed 5 µm (polystyrene and polyethylene) MPs for 5 days. The effects on viability, growth, and macrophage differentiation were evaluated after exposures. It was found that the growth of THP-1 cells was significantly reduced by high-dose MP exposures, independent of particle size or type. Interestingly, this suppression of THP-1 cell growth was not accompanied by significant alterations to cell viability with either the 1 µm, 5 µm, or mixed MPs at any of the doses investigated. Additionally, the impacts of MP exposure on the macrophage differentiation of THP-1 cells were also evaluated. This study provides novel information regarding the immunotoxicity of MPs, which is critical information for understanding the health impacts of these persistent and ever-increasing environmental pollutants. *This work was supported by National Institute of General Medical Sciences (NIGMS) of the National Institutes of Health (NIH) Grant Number 1R16GM146669-01 and Institutional Development Award (IDeA) P20 GM103451.*

* **Longitudinal Study of Carcinogenic Metals in Navajo Children from the Navajo Birth Cohort Study**

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Abstract:
There are over 500 abandoned uranium mines across the Navajo Nation, exposing communities to environmental metals known to act as carcinogens. Exposure to carcinogens at early-life stages have been shown to increase the likelihood of developing cancer later on. Children are at a developmental stage in life where they may be more susceptible to effects later in life. The current study identified and analyzed metal exposures in longitudinal samples from 556 children enrolled in the Navajo Birth Cohort Study (NBCS). Concentrations of uranium (UUR), total arsenic (UTAS), dimethylarsinic acid (UDMA), monomethylarsinic acid (UMMA), and arsenous III acid (UAS3) were assessed longitudinally between birth to 5 years of age. The goals of this study were to (i) compare metal concentration levels in children to the national average found in adults, (ii) identify the changes in metal concentrations overtime, (iii) identify the overall distribution of metal concentration, and iv) determine patterns of exposure (i.e. chronic or acute) in longitudinal samples. Findings demonstrate early life exposures to metals known to contribute to cancer incidence. Overall trends show increasing metal concentrations of uranium, arsenic, dimethylarsinic acid, monomethylarsinic acid, and arsenous III acid in children over the time period tested. It is especially concerning that the measured metal concentrations are at or approaching average adult concentrations as reported by the National Health and Examination Survey (NHANES). These results can guide future health initiatives in Navajo communities as well as to initiate research to better

understand exposure sources and identify mitigation approaches to reduce early life exposures to toxic metals.

* **Urinary Arsenic, Polycyclic Aromatic Hydrocarbons, and Metal Exposure and Risk of Stroke**

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Abstract:
Exposure to chemicals or metals from various environmental and occupational settings has been associated with adverse health conditions such as cardiovascular diseases, pulmonary diseases, and cancers. Exposure to environmental chemicals can occur from contaminated food, water, inhalation (lung), and absorption (skin). Stroke is one of the primary causes of morbidity and mortality worldwide. In addition, Stroke is a leading cause of death and long-term disability in the United States. Limited studies are conducted to assess the impact of polycyclic aromatic hydrocarbons, arsenic, and other metals exposure and their association with the risk of stroke. This study aimed to assess seven species of urinary arsenic (arsenous acid, arsenic acid, arsenobetaine, arsenocholine, dimethylarsinic acid, monomethylarsonic acid, and total arsenic), seven types of urinary polycyclic aromatic hydrocarbons (PAHs) compounds (1-hydroxynaphthalene, 2-hydroxynaphthalene, 3-hydroxyfluorene, 2-hydroxyfluorene, 1-hydroxyphenanthrene, 1-hydroxypyrene, 2 & 3-hydroxyphenanthrene) and 14 types of urinary metals (cadmium, barium, cobalt, molybdenum, mercury, cesium, manganese, antimony, lead, tin, strontium, tungsten, thallium, and uranium) and their association with those who reported having been told they had had a stroke by a medical professional. We performed a cross-sectional analysis using the 2011-2012, 2013-2014, and 2015-2016 National Health and Nutrition Examination Survey (NHANES) data. Data from approximately 5,537 adults aged 20 years and older were analyzed using logistic modeling of the complex weighted survey design. R version 3.6.3 software has been used to conduct the analyses. Among demographic variables, age 45 years and above, being a college graduate, a depression score of 5-9, and more than 100 lifetime cigarettes smoked were significantly associated with greater risks of stroke among the study population. A family income to poverty ratio of 1.5 and above, being born in a country other than the US, being uninsured, and being never married were inversely associated with having had a stroke. Four species of urinary PAHs, including the third quantiles of 1-hydroxynaphthalene [odds ratio (OR): 2.327, 95% confidence interval (CI): 0.961-5.632], 2-hydroxynaphthalene [OR: 2.449, 95% CI: 1.067-5.622] and 3-hydroxyfluorene [OR: 2.289, 95% CI: 1.077-4.861] and the second quantiles of 3-hydroxyfluorene [OR: 2.201, 95% CI: 1.115, 4.346] and 1-hydroxypyrene [OR: 2.066, 95% CI: 1.037, 4.114] showed a positive correlation with increased odds of stroke. Among metals, the third [OR: 3.566, 95% CI: 1.370, 9.280] and fourth [OR: 2.844, 95% CI: 0.947, 8.543] quantiles of urinary manganese showed a positive correlation with increased odds of stroke. The study observed that urinary PAHs and manganese are significantly associated with stroke. Future studies in humans are suggested to support or refute this finding.

* **Arsenic, Polycyclic Aromatic Hydrocarbons, and Metal Exposure and Association of Cancers among Women**

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Abstract:

In the United States, cancers that most often affect women are breast, colorectal, uterine, lung, cervical, skin, and ovarian cancers. Environmental pollutants may have a significant role in both the initiation and progression of various types of cancers among women. However, limited study has been conducted on this issue. This study aimed to assess seven species of arsenic, seven types of polycyclic aromatic hydrocarbon (PAH) compounds, and fourteen types of metals (cadmium, barium, cobalt, molybdenum, mercury, cesium, manganese, antimony, lead, tin, strontium, tungsten, thallium, and uranium) concentrations in urine and their correlation for cancer among women. We performed a cross-sectional analysis of the 2011-2012, 2013-2014, and 2015-2016 National Health and Nutrition Examination Survey (NHANES) data using logistic modeling of the complex weighted survey design. Data from 4,956 women aged 40 years and older were analyzed. The statistical analysis was done using "R" version 4.0.4 software. In the demographic variables, educational levels of high school and beyond and age groups 50 years and above were significantly associated with higher odds of breast cancer. In the race/ethnicity category, non-Hispanic Blacks had higher odds of having both uterine and cervical cancers. Hispanics other than Mexicans, women aged 70 years and older, widowed, and those who smoked more than 100 cigarettes in a lifetime had significantly higher odds of developing cervical cancer. Five types of urinary PAHs, including second and third quantiles of 1-hydroxynaphthalene [odds ratio (OR): 13.372, 95% confidence interval (CI): 1.218, 146.829 and OR: 40.686, 95% CI: 4.670, 354.466], third quantile of 3-hydroxyfluorene [OR: 4.256, 95% CI: 1.105, 16.394], third quantile of 1-hydroxyphenanthrene [OR: 11.892, 95% CI: 1.405, 100.672] and second and third quantiles of 1-hydroxypyrene [OR: 18.927, 95% CI: 2.377, 150.675 and OR: 27.103, 95% CI: 1.667, 440.642] showed positive associations with increased odds of uterine cancer. Among metals, second [OR: 21.998, 95% CI: 2.067, 234.078] and third [OR: 28.753, 95% CI: 2.973, 278.041] quantiles of urinary cobalt showed positive associations with increased odds of uterine cancer. Second quantiles of arsenocholine [OR: 4.447, 95% CI: 1.394, 14.181] and total arsenic [OR: 4.717, 95% CI: 1.267, 17.563] showed positive associations with increased odds of uterine cancer. The study observed that five urinary types of PAHs, cobalt, arsenocholine, and total arsenic, are significantly associated with uterine cancer among women. Further studies in humans are suggested to support or refute this finding.